Claims

1. A method for evaluating the cardiovascular effect of a candidate agent, comprising the steps of:

(a) contacting an estrogen receptor-enhanced vascular endothelial cell with a candidate agent; and

(b) determining whether the candidate agent modulates expression of at least one estrogen-regulated marker, wherein the expression of the marker is previously determined to be induced by estrogen in estrogen receptor-enhanced vascular endothelial cells, and therefrom determining whether the candidate agent has a cardiovascular effect.

2. A method according to claim 1, wherein the cell is immortalized.

3. A method according to claim 1, wherein step (b) comprises the steps of:

(i) detecting a level of an estrogen-regulated marker; and

(ii) comparing the detected level of the estrogen-regulated marker with a level of the estrogen-regulated marker in the absence of the candidate agent.

4. A method according to claim 1, wherein step (b) comprises the steps of:

(i) detecting a level of mRNA encoding an estrogen-regulated marker; and

(ii) comparing the detected level of mRNA encoding the estrogen-regulated marker with a level of mRNA encoding the estrogen-regulated marker in the absence of estrogen-related compound.

5. A method according to claim 4, wherein the level of mRNA is detected using an Rnase protection assay.

6. A method according to claim 4, wherein the level of mRNA is detected by:

preparing cDNA from mRNA present within the cell; and

amplifying mRNA encoding the estrogen-regulated marker via polymerase chain reaction.

7. A method according to claim 6, wherein the amplification is performed using real-time PCR analysis.

8. A method according to claim 1, wherein the cell is transfected with a polynucleotide comprising a promoter for an estrogen-regulated marker, operably linked to a reporter gene.

9. A method according to claim 8, wherein step (b) comprises the steps of:

(i) detecting a level of reporter protein activity; and

(ii) comparing the level of reporter protein activity detected with a level of reporter protein in the absence of candidate agent.

10. A method according to claim 8, wherein step (b) comprises the steps of:

(i) detecting a level of reporter mRNA; and

(ii) comparing the level of reporter mRNA detected with a level of reporter mRNA in the absence of estrogen-related compound.

11. A method according to claim 1, wherein the ability of the candidate agent to modulate expression of at least two estrogen-regulated markers is determined.

12. A method according to claim 1, wherein the estrogen-regulated marker is selected from the group consisting of SEQ ID NOs:1-74.

13. A method for identifying a selective estrogen receptor modulator (SERM), comprising the steps of:

(a) contacting at least two different cells that express an estrogen-regulated marker expression with a candidate SERM;

(b) determining levels of expression of at least one estrogen-regulated marker in the cells; and

(c) comparing the levels of expression with levels of expression of the estrogen-regulated marker(s) in cells following contact with estrogen, and therefrom determining whether the candidate SERM is a selective estrogen receptor modulator.

14. A method according to claim 13, wherein the estrogen-regulated marker is selected from the group consisting of SEQ ID NOs:1-74.

15. A method according to claim 13, wherein levels of at least two estrogen-regulated markers are determined.

16. A method according to claim 13, wherein each of the cells is independently selected from the group consisting of bone, urogenital, cardiovascular, breast, ovarian, endometrial, and central nervous system cells.

17. A method according to claim 13, further comprising the steps of:

(d) contacting breast cells that express an estrogen-regulated marker expression with estrogen and a candidate SERM;

(e) determining levels of expression of at least one estrogen-regulated marker in the breast cells; and

(f) comparing the levels of expression with levels of expression of the estrogen-regulated marker(s) in the breast cells following contact with estrogen, in the absence of candidate SERM.

18. A method for inhibiting the development of a cardiovascular disease in a patient; comprising administering to a patient an agent identified according to the method of claim 1 or a SERM identified according to claim 13.

19. A method for inhibiting the development of breast cancer in a patient; comprising administering to a patient a SERM identified according to the method of claim 17, wherein the SERM inhibits induction of estrogen-regulated marker expression by estrogen in breast cells.

20. A method for inhibiting the development of osteoporosis in a patient; comprising administering to a patient a SERM identified according to claim 13.

21. An isolated or recombinant nucleic acid comprising SEQ ID NO: 56; SEQ ID NO: 57; SEQ ID NO: 58; SEQ ID NO: 59; SEQ ID NO: 60; SEQ ID NO: 61; SEQ ID NO: 62; SEQ ID NO: 63; SEQ ID NO: 64; SEQ ID NO: 65; SEQ ID NO: 66; SEQ ID NO: 67; SEQ ID NO: 68; SEQ ID NO: 69; SEQ ID NO: 70; SEQ ID NO: 71; SEQ ID NO: 72; SEQ ID NO: 73; SEQ ID NO: 74; or SEQ ID NO: 75.

22. An isolated or recombinant nucleic acid that hybridizes under stringent conditions to the nucleic acid of SEQ ID NO: 56; SEQ ID NO: 57; SEQ ID NO: 58; SEQ ID NO: 59; SEQ ID NO: 60; SEQ ID NO: 61; SEQ ID NO: 62; SEQ ID NO: 63; SEQ ID NO:

64; SEQ ID NO: 65; SEQ ID NO: 66; SEQ ID NO: 67; SEQ ID NO: 68; SEQ ID NO: 69; SEQ ID NO: 70; SEQ ID NO: 71; SEQ ID NO: 72; SEQ ID NO: 73; SEQ ID NO: 74; or SEQ ID NO: 75.

23. An isolated or recombinant nucleic acid that is at east 75% identical to at least 50 consecutive nucleic acids of SEQ ID NO: 56; SEQ ID NO: 57; SEQ ID NO: 58; SEQ ID NO: 59; SEQ ID NO: 60; SEQ ID NO: 61; SEQ ID NO: 62; SEQ ID NO: 63; SEQ ID NO: 64; SEQ ID NO: 65; SEQ ID NO: 66; SEQ ID NO: 67; SEQ ID NO: 68; SEQ ID NO: 69; SEQ ID NO: 70; SEQ ID NO: 71; SEQ ID NO: 72; SEQ ID NO: 73; SEQ ID NO: 74; or SEQ ID NO: 75.

24. The nucleic acid of claim 23, that is at least 85% identical to at least 50 consecutive nucleic acids SEQ ID NO: 56; SEQ ID NO: 57; SEQ ID NO: 58; SEQ ID NO: 59; SEQ ID NO: 60; SEQ ID NO: 61; SEQ ID NO: 62; SEQ ID NO: 63; SEQ ID NO: 64; SEQ ID NO: 65; SEQ ID NO: 66; SEQ ID NO: 67; SEQ ID NO: 68; SEQ ID NO: 69; SEQ ID NO: 70; SEQ ID NO: 71; SEQ ID NO: 72; SEQ ID NO: 73; SEQ ID NO: 74; or SEQ ID NO: 75.

25. The nucleic acid of claim 24, that is at least 95% identical to at least 50 consecutive nucleic acids SEQ ID NO: 56; SEQ ID NO: 57; SEQ ID NO: 58; SEQ ID NO: 59; SEQ ID NO: 60; SEQ ID NO: 61; SEQ ID NO: 62; SEQ ID NO: 63; SEQ ID NO: 64; SEQ ID NO: 65; SEQ ID NO: 66; SEQ ID NO: 67; SEQ ID NO: 68; SEQ ID NO: 69; SEQ ID NO: 70; SEQ ID NO: 71; SEQ ID NO: 72; SEQ ID NO: 73; SEQ ID NO: 74; or SEQ ID NO: 75.